General

Guideline Title

Molecular testing for cystic fibrosis carrier status practice guidelines: recommendations of the National Society of Genetic Counselors.

Bibliographic Source(s)

Langfelder-Schwind E, Karczeski B, Strecker MN, Redman J, Sugarman EA, Zaleski C, Brown T, Keiles S, Powers A, Ghate S, Darrah R. Molecular testing for cystic fibrosis carrier status practice guidelines: recommendations of the National Society of Genetic Counselors. J Genet Couns. 2014 Feb;23(1):5-15. [74 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Langfelder-Schwind E, Kloza E, Sugarman E, Pettersen B, Brown T, Jensen K, Marcus S, Redman J. Cystic fibrosis prenatal screening in genetic counseling practice: recommendations of the National Society of Genetic Counselors. J Genet Couns. 2005 Feb;14(1):1-15.

Recommendations

Major Recommendations

Recommendation 1: Counseling about Cystic Fibrosis (CF) and the *cystic fibrosis transmembrane conductance regulator (CFTR)*-related Disease Spectrum

While most positive CF carrier screening results identify mutations associated with classic CF disease, genetic counselors offering CF carrier screening should ensure that they are providing the most current information to patients regarding the range of symptoms, potential treatment options, and quality of life issues associated with CF and the *CFTR*-related disease spectrum.

Recommendation 2: To Whom Should Carrier Testing for CF Be Offered?

Carrier testing for CF should be offered to all women of reproductive age, regardless of ancestry; preferably preconceptionally. CF carrier testing should also be offered to any individual with a family history of CF and to partners of mutation carriers and people with CF.

Recommendation 3: Pre-test Risk Assessment

Pre-test risk assessment should include an estimate of CF carrier frequency based on the individual's family history, ethnic background, and the predicted residual risk to have a child with CF if the test is negative.

Recommendation 4: CF Carrier Test Selection

Carrier testing panels should include the mutations recommended by the College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics (ACMG). For individuals of non-Northern European descent, pan-ethnic panels that include additional mutations more commonly identified in minority populations are appropriate to consider. Focus general population CF screening practices on identifying carriers of established disease-causing *CFTR* mutations.

Recommendation 5: Changes in Testing Panels and Interpretation

The inclusion and exclusion of mutations on available *CFTR* mutation screening panels remains a dynamic process as new information is learned about the pathogenicity of *CFTR* mutations. When individuals present for genetic counseling with prior carrier screening results, those results should be reviewed and re-interpreted, if necessary, in light of current knowledge.

Recommendation 6: Communicating Negative and +/− Carrier Screening Results

Clients who have had a negative CF carrier screening test result should be informed of their reduced or residual risk to have a child with cystic fibrosis, and the possibility of their child having an abnormal CF newborn screen if one partner is a CF carrier.

Recommendation 7: Counseling Couples at Risk to Have a Child with CF

When both parents are known carriers for CF, available prenatal and pre-implantation diagnostic testing should be offered. Prenatal facilitation of a monitoring plan should begin for couples at risk or who continue a pregnancy known to have CF, and postnatal evaluation through sweat testing and state newborn screening (NBS) programs, should be discussed.

Recommendation 8: The R117H/Poly T and 5T/Thymidine/Guanine (TG) Tract Alleles

If a client is found to carry an R117H mutation, it is important to ensure the testing laboratory performs reflex testing for poly T status along with studies to determine the *cis/trans* orientation of the poly T alleles. In the absence of an R117H mutation, assessment of the intron 8 poly T or TG tracts is not recommended for routine CF carrier testing.

Recommendation 9: Individuals with ≥2 Mutations Identified by Carrier Screening

Identification of two or more mutations in a patient referred for routine carrier screening should lead to a referral for clinical diagnostic evaluation. If the mutations identified are uncommon *CFTR* sequence variants, the likelihood of pathogenicity may be refined through determination of phase (*cis/trans* orientation).

Recommendation 10: CF Genotype/Phenotype Correlations

While some broad correlations can be made between genotype and anticipated phenotype, genetic counselors should not counsel regarding severity of disease course based on published case reports or individual patient experience.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Cystic fibrosis

Guideline Category

Counseling

Diagnosis

Risk Assessment

Screening

Clinical Specialty

Family Practice

Medical Genetics

Obstetrics and Gynecology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Social Workers

Guideline Objective(s)

- To provide practice recommendations for genetic counselors whose clients are considering cystic fibrosis (CF) carrier testing or seeking information regarding CF molecular test results
- To provide updated information about the natural history, diagnosis, and treatment of CF and related conditions
- To supplement genetic counselors' knowledge and understanding of the available carrier screening and diagnostic testing options
- To describe the current state of genotype/phenotype correlations for *CF transmembrane conductance regulator (CFTR)* mutations and an approach to interpreting both novel and previously described variants
- To provide a framework for genetic counselors to assist clients' decision-making regarding CF carrier testing, prenatal diagnosis, and pregnancy management

Target Population

- Pregnant women and their partners, and couples planning a pregnancy
- Individuals who are considering cystic fibrosis (CF) carrier testing or who are seeking information regarding CF molecular test results

Interventions and Practices Considered

1. Genetic counseling about cystic fibrosis (CF)
2. Carrier testing for CF for all women of reproductive age
3. Pre-test risk assessment based on family history, ethnic background, and predicted residual risk to have a child with CF
4. CF carrier testing based on included mutations
5. Counseling of couples at risk to have a child with CF
6. Reflex testing for poly T status
7. Referral for clinical diagnostic evaluation

Major Outcomes Considered

- Risk of cystic fibrosis (CF)
- Mutation detection rate
- Effectiveness of genetic counseling
- Strength of genotype/phenotype correlations

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The guideline authors searched the PubMed database in 2010, 2011, 2012, and 2013 using the terms cystic fibrosis diagnosis, sweat test, cystic fibrosis practice guidelines, cystic fibrosis genotype/phenotype, cystic fibrosis newborn screening, cystic fibrosis carrier screening, and cystic fibrosis genetic counseling. English-language papers published in the United States and abroad were reviewed.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Not stated

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review

Description of the Methods Used to Analyze the Evidence

Each practice guideline focuses on a clinical or practice-based issue, and is the result of a review and analysis of current professional literature believed to be reliable.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The practice guidelines were developed by members of the National Society of Genetic Counselors (NSGC).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of molecular testing for determination of cystic fibrosis carrier status

Potential Harms

- In cases where one member of a couple has been identified as a cystic fibrosis (CF) carrier and the second has had negative carrier test results, the counseling issues may become more challenging. Framing the residual risk in alternative formats may be helpful. Some patients may have negative emotional, cognitive, and/or behavioral responses to information they find to be ambiguous, and it can be helpful to explore feelings and perceptions about what it would be like to have a child with CF. It is also important to explore whether there are moral, religious, or cultural factors playing a role in the response.
- Informing patients about the role CF newborn screening in identifying CF patients with rare mutations and preparing patients for the potential to have a (likely false) positive CF newborn screen if their newborn carries one mutation may help to alleviate post-partum concerns.

Qualifying Statements

Qualifying Statements

- The practice guidelines of the National Society of Genetic Counselors (NSGC) are developed by members of the NSGC to assist genetic counselors and other health care providers in making decisions about appropriate management of genetic concerns, including access to and/or delivery of services. Each practice guideline focuses on a clinical or practice-based issue, and is the result of a review and analysis of current professional literature believed to be reliable. As such, information and recommendations within the NSGC practice guidelines reflect the current scientific and clinical knowledge at the time of publication, are only current as of their publication date, and are subject to change without notice as advances emerge.

- In addition, variations in practice, which take into account the needs of the individual patient and the resources and limitations unique to the institution or type of practice, may warrant approaches, treatments and/or procedures that differ from the recommendations outlined in this guideline. Therefore, these recommendations should not be construed as dictating an exclusive course of management, nor does the use of such recommendations guarantee a particular outcome. Genetic counseling practice guidelines are never intended to displace a health care provider's best medical judgment based on the clinical circumstances of a particular patient or patient population.
- Practice guidelines are published by NSGC for educational and informational purposes only, and NSGC does not "approve" or "endorse" any specific methods, practices, or sources of information.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2005 Feb (revised 2014 Feb)

Guideline Developer(s)

National Society of Genetic Counselors - Medical Specialty Society

Source(s) of Funding

National Society of Genetic Counselors

Guideline Committee

Not stated

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Not stated

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Guideline Availability

Electronic copies: Available to subscribers from the Journal of Genetic Counseling Web site .

Print copies: Available from the National Society of Genetic Counselors, 233 Canterbury Drive, Wallingford, PA 19086-7608; Web site: www.nsgc.org .

Availability of Companion Documents

The following is available:

- Bennett RL, French KS, Resta RG, Doyle DL. Standardized human pedigree nomenclature: update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Couns 2008 Oct;17(5):424-33. Available to subscribers from the Journal of Genetic Counseling Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on March 22, 2006. The information was verified by the guideline developer on May 3, 2006. This NGC summary was updated by ECRI Institute on January 27, 2014. The updated information was verified by the guideline developer on February 17, 2014.

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